POSTER SESSION

1033 Vascular Pathology and Inflammation

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

1033-134 High Body Iron Stores Predispose for Early Vascular Modifications in B-Thalassemia Major Patients

Ioannis E. Kallikazaros, Constantinos Tsioufis, Anastasios Spanos, Panagiotis Zambaras, Christodoulos Stefanadis, Pavlos Toutouzas, Hippokration Hospital, Athens, Greece

Background: Although previous studies have been reported that increased serum ferritin levels were associated with an excess risk of acute myocardial infarction, several questions regarding the relation of increased body iron stores with the atherosclerotic process remain in question.
Methods: For this purpose, we investigated the relation of early carotid atherosclerotic changes to body iron status on B-Thalassemia major patients, a population with chronic iron overload. Intima-media thickness (IMT) of the common carotid artery (CCA) was evaluated by high resolution B-mode Ultrasonography (Biosound 2000 II Sa) in 45 B-Thalassemia major patients (mean age 16±4 years). Our subjects were free from any known risk factors for cardiovascular disease. Body iron status was assessed by the mean serum concentration of ferritin in the last five years. The findings were compared to those obtained from 20 age and sex matched normal individuals.
Results: IMT of CCA in b-Thalassemia patients was 0.78±0.1 mm while in normal subjects was 0.54±0.2 mm (p<0.001). Mean serum level of ferritin in the last five years in the b-Thalassemia patients was 2720±1980 ng/ml and in normal subjects was 105±45 ng/ml (p<0.001). There was a strong positive correlation between IMT of CCA and level of ferritin in b-Thalassemia group (r=0.82, p<0.005).
Conclusion : The IMT of the CCA increased in proportion to the increased serum levels of ferittin. These data provide evidence that the body iron status plays an important role in the progress of early atherosclerotic changes. However, further studies are required to investigate the effects of multiple blood transfusions to cerebrovascular complications associated with b-Thalassemia major patients.

1033-135 Clustering of Acute Phase Markers With Inflammatory Implications

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Background: The reported acute-phase characteristics of thrombotic factors, specifically Lp(a), homocysteine (hcy) and fibrinogen, may suggest their conjoint serum elevation (in the chronic clinical setting) as representing a generalized inflammatory state. Advanced traditional Framingham risk known to be correlated with enhanced inflammation should reveal an association with thrombotic factors of inflammatory etiology. Methods: Data from an outpatient preventive cardiology clinic (n=2969) include traditional risk (Framingham) and known biochemical risk markers (Hcy, Fib & Lp(a); hsCRP in a sub cohort (n=742)). Clustering was examined using a binomial expansion based on individual risk of each marker.
Results: These three thrombotic factors tended to be more clustered than would be expected under the assumption of independence (p<0.001). Median Framingham global risk score increased from 4.5 when none of the three thrombotic factors were expressed to 8.0 when all three were expressed (p<0.001). In the highest tertile of Framingham risk, 3.5 times as many patients as expected had all three thrombotic risk factors present, and 30% more patients than expected had "0" thrombotic features when Framingham risk was in the bottom tertile (p<0.001). Finally, hsCRP was high (>0.15 mg/dL) in 95% of subjects with all 3 factors compared to 53% when none were expressed (p<0.001).
Conclusion: High Framingham risk predicts a 3-fold enhancement in the probability of exhibiting an increase in all 3 thrombotic markers. Clustering of these thrombotic factors, particularly in the high traditional risk setting, along with coincident enrichment in serum CRP, describes a generalized inflammatory condition in stable patients.

1033-136 Experimental Exposure to Carbon Particles Does Not Cause Adverse Changes in Cardiac Autonomic Control or a Systemic Inflammatory Response in Human Subjects

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Background: Epidemiology has demonstrated an association between cardiovascular admissions and mortality and daily changes in levels of particulate air pollutants. Two mechanisms have been suggested:1) Pulmonary injury and a systemic inflammatory response, increasing the risk of plaque rupture and thrombosis; 2) Adverse effects on cardiac autonomic control, mediated via airway receptors increasing the risk of arrhythmia. While observational evidence from population studies supports these hypotheses, this is the first human challenge study to measure the cardiovascular response to known concentrations of specific pollutants.
Methods: In a random order, double blind, crossover study using a head dome exposure system, 12 healthy volunteers were exposed for 1 hour to air or air + carbon particles ($100\mu g/m^3$). High resolution C-reactive protein (hrCRP), markers of coagulation and heart rate variability (HRV) indexes during controlled respiration were measured before, immediately and 4 hours after exposure. **Results**: No significant changes were seen in any blood or HRV index in response to carbon, or in similar studies using sulphur dioxide (SO_2) ± carbon. **Conclusion:** In healthy volunteers, exposure to pure carbon particles or SO_2 does not adversely affect cardiac autonomic control or cause systemic inflammation. Thus the effects seen with ambient pollutants are likely to be attributable to reactive species on the particle surface. Studies are ongoing with these pollutants and in at-risk groups.

Results: Air versus *Carbon* (group mean ± SEM)

	Baseline	Post exposure	4 hours	24 hours
hrCRP (mg/l)	2.61 ± 0.70 vs *1.88 ± 0.46*	2.63 ± 0.67 vs *1.83 ± 0.43*	2.56 ± 0.65 vs *1.85 ± 0.46*	2.40 ± 0.62 vs *1.55 ± 0.33*
Fibrinogen (g/l)	2.99 ± 0.21 vs *2.83 ± 0.16*	3.18 ± 0.26 vs *2.90 ± 0.18*	2.92 ± 0.25 vs *2.80 ± 0.14*	3.49 ± 0.21 vs *3.13 ± 0.18*
SDNN (ms)	29.1 ± 3.9 vs *32.5 ± 3.2*	35.2 ± 3.8 vs *53.6 ± 8.3*	29.4 ± 5.4 vs *29.7 ± 3.1*	

1033-137 Matrix Metalloproteinase Genetic Polymorphisms in Premature Coronary Artery Disease

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Background: to what extent the genetic variation in human matrix metalloproteinases (MMPs) is associated with acute coronary syndromes (ACS) in young males has not been determined as yet.
Methods: we investigated the following three polymorphisms: 1) functional 5A/6A promoter polymorphism in the Stromelysin-1 (MMP-3) gene, 2) functional C/T promoter polymorphism in the Gelatinase B (MMP-9) gene, 3) A/G exon-6 polymorphism in the MMP-9 gene. We genotyped 401 men aged below 55 years: 200 patients with documented ACS (either previous myocardial infarction or unstable angina with angiographic evidence of ischemic heart disease) and 201 age-matched controls. Plasma citrate concentration of gelatinase B and stromelysin-1 along with gelatinase B plasma total activity were evaluated in a subgroup of 80 patients and 40 controls.
Results: patients showed higher prevalence of hypertension, hypercholesterolemia, diabetes, smoking habit, family history (all p< 0.0001) and a higher level of C reactive protein (p<0.0003). Differences in the genotype distribution between patients and controls are depicted in table 1. We found no relation between MMP genotypes distribution and extension of angiographic lesions in 147 premature coronary artery disease patients who underwent angiography. MMP genotypes did not influence their respective plasma levels either in patients or controls.
Conclusion: genetic variation in human MMP-3 and MMP-9 genes is not a major determinant of premature coronary artery disease.

Table I

Genotypes	Patients [200]	Controls [201]	P
MMP-3 5A/6A			0.979
5A5A	59 (29.5%)	59 (29,3)	
5A6A	91 (45.5%)	90 (44.8)	
6A6A	50 (25.0%)	52 (25.9%)	
6A allele frequency	0.48	0.48	
MMP-9 C/T			0.901
CC	136 (68.0%)	135 (67.2%)	
CT	62 (31.0%)	63 (31.3)	
TT	2 (1.0%)	3 (1.5%)	
T allele frequency	0.16	0.17	
MMP-9 A/G			0.689
AA	85 (42.5%)	94 (46.8%)	
AG	94 (47.0%)	87 (43.3%)	
GG	21 (10.5%)	20 (9.9%)	
G allele frequency	0.34	0.31	

1033-138 Obesity Is Associated With Systemic Inflammation Independent of Metabolic Cardiac Risk Factors in Healthy Young Adults

Michael J. Williams, Richie Poulton, Sheila Williams, University of Otago, Dunedin, New Zealand

Background: Obesity is associated with an increased risk of cardiovascular disease. Elevations of C-reactive protein (CRP) have recently been shown to be independently predictive of future cardiovascular events. Elevated CRP has also been associated with central obesity, and other features of the metabolic syndrome. This study aimed to assess the relationship between CRP and obesity in healthy young adults.
Methods: CRP, non-fasting total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, Lp(a) lipoprotein [Lp(a)],blood pressure, fitness (VO_2max), socioeconomic status, smoking status and anthropometric measurements were determined in 828 men and women aged 26 years.
Results: C-reactive protein levels (mg/L) according to obesity, adjusted for sex, child-

hood and adult socio-economic position (Model 1) and for total cholesterol, HDL, triglycerides, apolipoprotein A1, apolipoprotein B, Lp (a), systolic and diastolic blood pressure, VO_2max and smoking (Model 3).

	Unadjusted	Model 1	Model 2
Normal (BMI=18.5-25.0) N=476	3.73	3.62	3.32
Overweight (BMI=25.1-30.0) N=255	3.89	4.12	3.97
Obese (BMI=30.1-35.0) N=75	6.04*	5.85*	5.24*
Very obese (BMI>35.0) N=22	10.41‡	8.72†	7.03*

differs from those in the normal range * p<0.05, † p<0.01, ‡ p<0.001
Conclusion: CRP is independently related to obesity in healthy young adults. Chronic inflammation may contribute to the increased risk of atherosclerotic disease associated with obesity.

1033-139 Estrogen Receptor Alpha Gene Polymorphism Is Associated With Coronary Artery Disease Severity

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Background: Estrogens have beneficial effects on the cardiovascular system partially mediated by estrogen receptor alpha (ERα). Alternations in ERα expression may affect the atheroprotective role of estrogens. We hypothesized that genetic variation in the regulatory region of the ERα gene is associated with the angiographic severity of CAD.
Methods: We studied 496 consecutive patients (72% men, 28% women) who had coronary angiography. Severity of CAD was assessed by: 1) the number of major coronary vessels with at least one >50% narrowing (NMCV); 2) the number of vessels with any narrowing (NCV); 3) the total number of narrowings (NN). The length of the dinucleotide repeat thymine & adenine (TA repeats) upstream of exon 1 of the ERα gene, was determined by PCR. The median number of TA repeats was used to categorize the population into 3 groups: long alleles genotype (both alleles ≥18 repeats), short alleles genotype (both alleles <18 repeats), and mixed genotype (short & long allele). Since the contribution of genetic factors is expected to be more prominent in younger subjects, patients were divided into younger and older groups, age≤55 (n=128) vs. age>55 (n=368). The relationship between TA length and the severity of CAD was assessed by analysis of covariance, stratified by age group. Sex and major CAD risk factors (diabetes, hypertension, hyperlipidemia, smoking, obesity, family history) were included as confounding factors.
Results: Young patients with long alleles genotype had a significantly greater number of narrowed coronary arteries compared to those with short alleles genotype (NCV 3.7±2.4 vs. 2.5±1.8, respectively, p<0.02). Similarly, young patients with long alleles had a higher total number of coronary narrowings compared to those with short alleles (NN 4.5±2.7 vs. 3.1±2.2, respectively, p<0.02). A trend towards a higher NMCV in young patients with long alleles was also observed (NMCV 2.0±1.1 vs. 1.6±0.9, long vs. short, p=NS). These differences were not observed in older patients.
Conclusion: The length of the TA dinucleotide repeat in the regulatory region of the ERα gene is associated with the angiographic severity of CAD in young subjects, independent of the major coronary risk factors.

POSTER SESSION

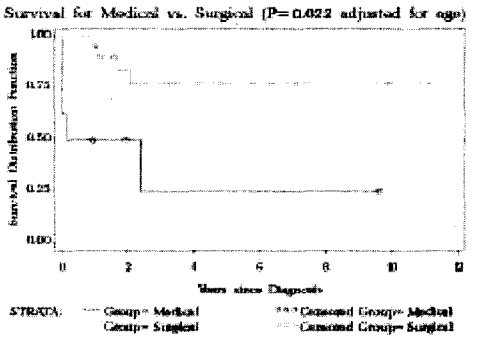
1034 Aortic Diseases: Prevention, Risk, and Repair

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

1034-140 Surgical Intervention Is Superior to Medical Therapy in the Management of Type A Aortic Intramural Hematoma

Kevin J. Mikielski, Andrew Thomas McRae, III, Marc S. Penn, Monvadi B. Srichai, Richard D. White, Richard A. Grimm, The Cleveland Clinic Foundation, Cleveland, OH

Background: Aortic intramural hematoma (AIH) is a variant of aortic dissection. The management of Type A AIH remains controversial. This study was performed to determine the optimal treatment strategy for Type A AIH.
Methods: Transesophageal echocardiography (TEE), computed tomography (CT), and magnetic resonance imaging (MRI) databases were queried for "intramural hematoma" and "AIH." Charts and imaging studies were reviewed to identify cases of Type A AIH. Patients with Marfan's disease, traumatic AIH, and penetrating aortic ulcer were excluded. Mortality was determined via Social Security Death Index.
Results: Thirty cases of Type A AIH were identified between April 1991 and July 2001. Diagnosis was made by TEE alone (n=13), CT or MRI alone (n=1), and a combination of TEE and CT or MRI (n=16). Mean age was 68 +/- 12 years and 53% of patients were female. Hypertension was present in 90% of cases and 80% presented with chest and/or back pain. Pericardial effusion and aortic regurgitation were present in 57% and 73% of cases, respectively. Surgical intervention (ascending aorta graft placement) was utilized in 22/30 (73%) cases. The in-hospital mortality rate was significantly lower with surgical intervention (0/22, 0% Versus 3/8, 38%, p=0.002). Patients treated with surgical intervention had a significantly lower mortality rate according to Kaplan-Meier survival curves (p=0.022).
Conclusion: We conclude that surgical intervention is superior to medical therapy in the management of Type A AIH.



1034-141 Coronary Artery Involvement in Patients With Acute Type A Aortic Dissection: Clinical Characteristics and In-Hospital Outcomes

Eduardo Bossone, Rajendra H. Mehta, Santi Trimarchi, Jeanna V. Cooper, Dean E. Smith, Arturo Evangelista, Truls Myrmel, Jae Oh, Christoph A. Neinaber, Kim A. Eagle, Eric M. Isselbacher, On behalf of the International Registry of Acute Aortic Dissection (IRAD) Investigators, University of Michigan, Ann Arbor, MI, Massachusetts General Hospital, Boston, MA

Background: The clinical characteristics and outcomes of patients with type A acute aortic dissection (AAD) with coronary artery involvement (CAI) have not been well studied. **Methods**: Accordingly, we evaluated 475 AAD patients enrolled in IRAD (1/97-12/01). CAI was defined as extension of AAD into the coronary ostia or compromise blood flow to any coronary artery caused by the dissection. **Results**: CAI occurred in 64 (13.5%) of AAD patients and affected all ages and both sexes equally. Hypertension (83% vs 68%, p=0.01) and diabetes (9.7% vs 3.3%, p=0.03) were more common in CAI patients, whereas other comorbid conditions were similar in the 2-groups. Presenting symptoms (chest pain, syncope, heart failure, hypotension, or neurological deficit) and chest Xray findings were similar in the 2 groups. Although, CAI patient were more likely to show new Q wave or ST elevation on ECG (16.7% vs 4.3%, p=0.001), these findings were present in only 1 of 6 CAI patients. Aortic arch involvement and presence of periaortic hematoma, aortic regurgitation and pericardial effusion were more common in CAI patients. In-hospital management and outcomes of the 2 groups were similar. Only myocardial ischemia or infarction occurred more frequently in CAI patients (table).

In-hospital Complications	Overall	With coronary involvement	Without coronary involvement	p-value
All Neurological deficits (%)	137 (30.4)	19 (31.1)	118 (30.3)	0.9
Coma/Altered Consciousness (%)	33 (8.3)	4 (7.3)	29 (8.5)	1.0
Myocardial ischemia/ infarction (%)	73 (16.6)	26 (44.8)	47 (12.3)	<.001
Mesenteric ischemia/ infarction (%)	24 (5.4)	3 (5.1)	21 (5.5)	1.0
Hypotension (%)	151 (33.9)	20 (33.9)	131 (33.9)	1.0
Mortality (%)	139 (29.3)	17 (26.6)	122 (29.7)	0.6

Conclusions: CAI occurs infrequently in AAD patients and contrary to popular belief is not associated with greater mortality compared to AAD patients without CAI. It is the presence of extensive type A dissection, more than just CAI, that predicts outcomes.

1034-142 Renal Failure on Presentation Predicts Morbidity and Mortality in Aortic Dissection

Joshua A. Beckman, Rajendra H. Mehta, Eduardo Bossone, Jeanna V. Cooper, Dean E. Smith, Udo Sechtem, Linda Pape, Patrick T. O'Gara, Brigham & Women's Hospital, Boston, MA

Background: Vascular complications in aortic dissection are common and augur adverse outcomes. In the setting of an acute aortic dissection (AAD), the importance of renal failure (RF) as an adverse prognostic indicator remains incompletely defined. We sought to determine the clinical correlates and complications of AAD associated with (RF).
Methods: The records of 1078 patients in IRAD were evaluated. RF was defined as a serum creatinine greater than 2.0 mg/dL on presentation or an increase of greater than 0.7 mg/dl from baseline. Chi squared analysis was performed on specific endpoints.
Results: RF was noted in 85 patients from IRAD (7.8%). Subjects with and without RF were similar in age (62 vs. 63 y) and sex (34.1 vs 31.3% female). The clinical presenta-